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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/576,101	05/22/2000	Andreas Suhrbier	FBRC:004USC1/HYL	3194

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EXAMINER	
HUYNH, PHUONG N	
ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 01/05/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/576,101	SUHRBIER ET AL.	
	Examiner	Art Unit	
	Phuong Huynh	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *Three* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 September 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *14,16-31,33 and 35* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *14, 16-31, 33 and 35* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *29 September 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

1. Claims 14, 16-31, 33 and 35 are pending.

2. In view of the amendment filed 9/29/03, the following rejections remain.

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 14, 16-26, 28-31, 33 and 35 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a recombinant vaccine CTL polyepitope-based composition comprising a polynucleotide encoding CTL epitopes as depicted in Figure 5 derived from pathogens MCMV, influenza, EBV, Adenovirus and EG7 tumor for use as vaccines, does not reasonably provide enablement for vaccine compositions and their use in vaccination against *any disease*. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in **scope** with these claims.

Factors to be considered in determining whether undue experimentation is required to practice the claimed invention are summarized *In re Wands* (858 F2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)). The factors most relevant to this rejection are the scope of the claim, the amount of direction or guidance provided, the lack of sufficient working examples, the unpredictability in the art and the amount of experimentation required to enable one of skill in the art to practice the claimed invention. The specification disclosure is insufficient to enable one skilled in the art to practice the invention as broadly claimed without an undue amount of experimentation.

The specification discloses only a polynucleotide comprising multiple (up to ten) murine CTL epitope as depicted in Figure 5 from pathogens listed in Table 2 on page 14 in which the pathogens are from Epstein Barr Virus, Influenza virus, Cytomegalovirus, and Adenovirus. The response to said CTL epitopes from different pathogens are restricted by individual's HLA class where said CTL epitopes are linked contiguously to a T helper cell epitope from Ovalbumin and a B cell epitope from plasmodium faliciparum in a linear fashion (See Fig 5, in particular) that

expressed in vaccinia virus vectors and uses to vaccinate mice against MCMV, influenza, EBV and EG7 tumor.

The specification does not teach how to make and use any polynucleotide comprising any nucleic acid sequence encoding *any* CTL epitopes for treating or preventing any disease, including HIV. The specification does not disclose how using a recombinant vaccinia vector containing a polynucleotide encoding CTL epitopes from Influenza, EBV, Cytomegalovirus, Adenovirus and EG7 tumor can be extrapolated to protect any disease including **HIV** infection. Further, there is insufficient evidence that nucleic acid (DNA) vaccine using CTL epitopes from Influenza, EBV, Cytomegalovirus as depicted in Fig. 5 can prevent any disease, including AIDS. Applicants have not disclosed "CTL epitopes" from any disease, including any tumor other than **murine** CTL epitopes from Epstein Barr Virus, Influenza Virus, Cytomegalovirus and Adenovirus depicted in Fig. 5 and listed in Table 2, in turn, can be used as a vaccine against any disease including HIV infection. The claimed invention of "Nucleic acid vaccine" as recited in claim 14, 16-26, 28-31, 33 and 35 comprising any polynucleotide comprising any nucleic encoding any plurality of CTL epitopes, much less prevention of any disease. A polynucleotide or nucleic acid vaccine comprising polynucleotide without SEQ ID NO has no structure, much less function, in turn would be useful as a vaccine against any disease. Further, there is insufficient guidance and in vivo working examples at the time the application was filed that any undisclosed nucleotide encoding any undisclosed CTL epitopes is effective for a vaccine against a plurality of pathogens, including HIV and any tumor. Reasonable correlation must exist between the scope of the claims and scope of enablement.

The specification has not enabled the breadth of the claimed invention in view of the teachings in the specification as filed. The lack of guidance in the specification as to which CTL epitopes from HIV are appropriate for nucleic acid vaccine against HIV infection is unpredictable and the amount of experimentation required to enable one of skill in the art to practice the claimed invention.

The state of the art is such that even though HIV vaccine research has been under way for 10 years, not a single vaccine has been demonstrated to be effective against AIDS (See page 1993 col. 3, last two paragraph, JAMA 282 (21): 1992-1994; PTO 892). Ramsay *et al* summarizes that "vaccine involving proteins or whole inactivated virions have not, to date, reliably induced either antibodies capable of neutralizing HIV or CTL responses, in human or non-human primates and

for reasons which remain unclear, even DNA vaccines do not appear to reliably induce CTL response in outbred primates" including humans (see page 31 column 2, in particular).

Verma *et al*, of record, teach that the problem of gene therapy is the inability to deliver genes efficiently to the right type of cell, obtaining sustained expression of the therapeutic protein and without triggering the host immune responses (See page 239, in particular). Therefore, in the absence of in vivo working examples, it would require undue experimentation of one skilled in the art to practice the claimed invention.

Reyes-Sandoval *et al*, of record, teach that "Although DNA vaccines induce significant immune responses in small animal trials their efficacy in humans has so far been less promising thus necessitating additional optimizations of this novel vaccine approach".

Tuteja *et al*, of record, teach that "There are several hurdles that need to be overcome on the road to the use of DNA vaccines widely. These include the technical challenges of improving delivery and/or potency so that low doses of DNA can achieve the efficacy of conventional vaccines.

Given the indefinite number of disease and in view of the insufficient number of in vivo working examples, the insufficient guidance in the specification, the breadth of the claims, and the unpredictable state of the art with respect to *DNA vaccine* against a plurality of undisclosed pathogens, it would require undue experimentation for one skilled in the art to practice the entire **scope** of the claimed invention.

Applicants' arguments filed 9/29/03 have been fully considered but are not found persuasive.

Applicants' position is that (1) applicants have amended claim 27. (2) A skilled artisan will recognize from the disclosure that any CTL epitope may be useful in the present invention. (3) Given the diverse nature of the CTL epitopes include in the exemplified polyepitope encoding construct, and the exemplified teaching of the success of the claimed polyepitope encoding constructs, applicants maintained that the specification as filed contained a sufficient written description to demonstrate possession of the invention now claimed.

However, claim 33 is still drawn to *any* nucleic acid vaccine comprising any nucleotide comprising any nucleic acid sequence encoding a plurality of CTL epitopes wherein each CTL epitope is free of peptide sequences naturally found to flank that undisclosed CTL epitope and wherein a plurality of CTL epitopes are contiguous. A polynucleotide or nucleic acid vaccine comprising polynucleotide without the nucleotide sequence (SEQ ID NO) has no structure, much

less function, in turn would be useful as a vaccine against any disease, including HIV. Further, there is insufficient guidance and working examples at the time the application was filed that any undisclosed nucleotide encoding any undisclosed CTL epitopes is effective for a vaccine against any disease, pathogens such as HIV given the functional diversity of CTL epitopes. Reasonable correlation must exist between the scope of the claims and scope of enablement. See Brenner v. Manson, 383 U.S. 519, 535-36, 148 USPQ 689, 696 (1966), noting that "a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion." A patent is therefore not a license to experiment. See enablement Guidelines available at www.uspto.gov.

5. Claims 14, 16-26, 28-31, 33 and 35 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention.

The specification does not provide adequate written description of the claimed invention. The legal standard for sufficiency of a patent's (or a specification's) written description is whether that description "reasonably convey to the artisan that the inventor had possession at the time of the ...claimed subject matter", Vas-Cath, Inc. V. Mahurkar, 19 USPQ2d 1111 (Fed. Cir. 1991). In the instant case, the specification does not convey to the artisan that the Applicants had possession at the time of invention of the claimed polynucleotides 14, 16-26, 28-31, and 33 and the nucleic acid vaccine recited in claim 33. The nucleic acid sequences recited in claims 14, 16-26, 28-31, 33 and 35 encompass a large genus of polynucleotides and vaccines. There is insufficient disclosure in the specification to reasonably conveys to the artisan that the inventors had possession of the claimed invention.

Applicant has described only a polynucleotide encoding multiple murine CTL epitopes from murine Cytomegalovirus, lymphocytic choriomeninigitis, influenza, EBV, Adenovirus, T helper cell epitopes from *Berghei circumsporozoite* and Ovalbumin, and B cell epitopes from *plasmodium falciparum* as disclosed in Table 2 expressed in a vaccinia viral vector depicted in Fig. 5. The specification further discloses that the CTL epitopes are arranged in tandem in a contiguous sequence and the said CTL epitopes are from **different** HLA alleles flanking by a B cell epitope from *plasmodium falciparum* (See Fig 5, in particular). The arrangement of the ten CTL epitopes within the construct is such that two CTL epitopes in tandem are from the same

MHC class I HLA alleles but from different pathogens (See Figure 5 and Table 2, in particular). The specification as filed does not adequately describe the claimed genus, which encompasses CTL epitopes other than the one depicted in Fig. 5 and listed in Table 2 such that one skilled in the art would conclude that applicants were in possession of the claimed invention.

With the exception of the specific polynucleotide encoding the specific CTL epitopes mentioned above for CTL assay, there is insufficient written description about the structure associated with function of *any* polynucleotide comprising any nucleic acid sequence encoding a plurality of undisclosed CTL epitopes wherein each CTL epitope is substantially free of peptide sequences naturally found to flank that CTL epitope and wherein at least any two of the plurality of any CTL epitopes are contiguous or spaced apart by any intervening sequence that does not comprises a methionine because any polynucleotide without the specific nucleic acid sequence or SEQ ID NO has no structure, much less function, in turn, would be useful as a nucleic acid vaccine against any pathogen such as AIDS. Since the polynucleotide encoding any undisclosed CTL epitopes is inadequately described, it follows that any vector comprising any undisclosed polynucleotide is not adequately described. It also follows that any nucleic acid vaccine is not adequately described.

Further, the specification discloses only polynucleotide encoding multiple murine CTL epitopes from murine Cytomegalovirus, lymphocytic choriomeningitis, influenza, EBV, Adenovirus, T helper cell epitopes from *Berghei circumsporozoite* and Ovalbumin, and B cell epitopes from *plasmodium falciparum* as disclosed in Table 2 expressed in a vaccinia viral vector as depicted in Fig. 5, one of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, Applicant was not in possession of the claimed genus as broadly claimed. *See University of California v. Eli Lilly and Co. 43 USPQ2d 1398.*

Applicant is directed to the Final Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

Applicants' arguments filed 9/29/03 have been fully considered but are not found persuasive.

Applicants' position is that (1) applicants have amended claim 27. (2) A skilled artisan will recognize from the disclosure that any CTL epitope may be useful in the present invention. (3) Given the diverse nature of the CTL epitopes include in the exemplified polyepitope encoding

construct, and the exemplified teaching of the success of the claimed polyepitope encoding constructs, applicants maintained that the specification as filed contained a sufficient written description to demonstrate possession of the invention now claimed.

However, claim 33 is still drawn to *any* nucleic acid vaccine comprising any nucleotide comprising any nucleic acid sequence encoding a plurality of CTL epitopes wherein each CTL epitope is free of peptide sequences naturally found to flank that undisclosed CTL epitope and wherein a plurality of CTL epitopes are contiguous. Further, there is inadequate written description about the specific disease or pathogen to be treated by the undisclosed nucleic acid or nucleic acid vaccine given the diverse nature of the CTL epitopes. There is insufficient written description about the structure of any polynucleotide and any undisclosed nucleic acid vaccine because the "CTL epitopes" without the nucleotide sequence, the corresponding amino acids sequence (SEQ ID NO:) have no structure, much less function. Further, the term "comprise" is open-ended. It expands the intervening sequence to include additional nucleotide at either of both ends. Not only the number of CTL epitope is not defined in claim 14, the term "comprising" is open-ended. It expands the polynucleotide to include additional nucleotides at either or both ends of the undisclosed CTL epitopes from a host of undisclosed pathogens. Further the "intervening sequence that does not comprise a methionine" as disclosed in the specification refers to the internal initiation sequence (i.e. the codon ATG associated with a Kozac sequence) between **nucleotide sequences** encoding each CTL epitope. Because the internal initiation sequence is omitted, the resulting polynucleotide encoding the fusion protein comprises a plurality of cytotoxic T epitopes encoded by the polynucleotide having the internal translation initiation sequences omitted should be contiguous and **not spaced apart** by any intervening sequence as recited in claim 35. Since the polynucleotide encoding any CTL epitopes is inadequately described, it follows that any vector and any nucleic acid vaccine comprising any undisclosed polynucleotide is not adequately described for use as a vaccine against pathogen such as HIV.

6. Claims 14, 16-31, and 33 are rejected under 35 U.S.C. 112, first paragraph, containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. **This is a new matter rejection.**

Claims 14, 16-31, and 33 as written represents a departure from the specification and the claims as originally filed because the specification on page 2, lines 10-16 (now paragraph 6 of the

substitute specification) and the claims as originally filed require that the polynucleotide encoding a plurality of cytotoxic T lymphocyte epitopes from one or more pathogens and wherein at least one sequence is "**substantially** free of sequences encoding the peptide sequences naturally found to flank the CTL epitopes".

Applicants' arguments filed 9/29/03 have been fully considered but are not found persuasive.

Applicants' position is that (1) claims 15 and 24 have been canceled, and claims 14, 24, 27 and 33 have been amended. (2) Support for new claim 14 is to be found inter alia in pending claim 14 and cancelled claim l 5. Support for new claims 24 and 27 are to be found in the corresponding pending claims 24 and 27. Support for new claim 33 is to be found inter alia in pending claim 33 and canceled claim 34. Support for new claim 35 is to be found inter alia in the description at paragraph 5 in relation to "minimal" epitopes are of sequences that flank the CTL epitopes; in Figure 1 and Figure 5 of the application as originally filed in relation to contiguous CTL epitopes', in Figure 5 in relation to intervening sequences e.g., the spacer sequence TS positioned between the epitopes YPHFMPTNL and SGPSNTPPEM; at paragraph 37 in relation to the absence of a methionine in the intervening sequence of the encoded polytope; and in the description at paragraphs 37 to 39 which demonstrates efficient expression of the claimed nucleic acid, processing of the encoded polytope protein to produce minimal CTL epitopes, and CTL recognition of the processed epitopes.

However, the specification on page 2, lines 10-16 (now paragraph 6 of the substitute specification) and the claims as originally filed require that the polynucleotide encoding a plurality of cytotoxic T lymphocyte epitopes **from one or more pathogens** and wherein at least one sequence is "**substantially free of sequences encoding the peptide sequences naturally found to flank the CTL epitopes**".

7. The non-statutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timeless extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cirri. 1993); *In re Long*, 759 F.2d 887, 225 USPQ 645 (Fed. Cirri. 1985); *In re Van Onramp*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

8. Claims 14, 16-31, 33 and 35 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over Claims 14-17, 19-34, 53 and 54 of USSN 09/957,107.

(1) Claim 14 of USSN 09576,107 recites a polynucleotide comprising a nucleic acid sequences encoding a plurality of CTL epitopes wherein each encoded CTL epitope is substantially free of sequences found naturally to flank that CTL epitope and wherein at least two CTL epitopes are restricted by the same HLA allele such that those epitopes are correctly processed to permit their HLA restricted presentation in a subject having that HLA allele (Species). Therefore, claim 14 of USSN 09576,107 is included in the instant claims 14, 16-31, 33 and 35 which drawn to a polynucleotide comprising a nucleic acid sequence encoding a plurality of CTL epitopes, wherein each CTL epitope is free of peptide sequences found to flank that CTL epitope and wherein a plurality of CTL epitopes are contiguous. The "such that those epitopes are correctly processed to permit their HLA restricted presentation in a subject having that HLA allele" is an inherent property of the polynucleotide

Further, since all CTL epitopes are from MHC class I, the spacing between epitopes is an obvious variation of the recombinant fusion protein encoded by the claimed polynucleotide. Further, the recitation of "at least two CTL epitopes" in claim 14 of USSN 09576,107 is an obvious variation of "a plurality of CTL epitopes" as recited in instant claim 14.

(2) Claims 16-17, 19, 20-27, and 29-32 of USSN 09576,107 are the same as that recited in the instant claims 16-17, and 20-31.

(3) Claim 35 of USSN 09576,107 recites a nucleic vaccine comprising a polynucleotide comprising (i) a nucleic acid sequence encoding a plurality of CTL epitopes wherein each encoded CTL epitope is substantially free of sequences found naturally to flank that CTL epitope and wherein at least two of the encoded epitopes are restricted by the same HLA alleles and (ii) an acceptable carrier, which is included in the claim 33 of instant application since claim 33 of

instant application recites a nucleic acid vaccine comprising a polynucleotide comprising a nucleic acid sequence encoding a plurality of CTL epitopes, wherein each encoded CTL epitope is substantially free of sequences found naturally to flank that CTL epitope and wherein a plurality of CTL epitopes are contiguous and an acceptable carrier.

(4) Claim 53 of USSN 09576,107 recites a polynucleotide comprising a nucleic acid sequence encoding a plurality of cytotoxic T lymphocyte (CTL) epitopes wherein each encoded CTL epitope is free of sequences found naturally to flank that CTL epitope and wherein a plurality of contiguous CTL epitopes are restricted by one or more HLA alleles such that the contiguous epitopes are correctly processed to permit their HLA restricted presentation and CTL induction in a subject having said one or more HLA alleles and claim 54 of USSN 09/576,107 recites a polynucleotide comprising a nucleic acid sequence encoding a plurality of contiguous cytotoxic T lymphocyte (CTL) epitopes restricted by one or more HLA alleles such that each epitope of said plurality of contiguous CTL epitopes is correctly processed to permit its Hl-A-restricted presentation and CTL induction in a subject having said one or more HLA alleles wherein each encoded CTL epitope is free of sequences found naturally to flank that CTL epitope. Both claims 53 and 54 would include claim 35 of instant application since the protein processing and effective HLA-restricted presentation and CTL induction are inherent properties of the polypeptide encoded by the claimed polynucleotide.

Since the claims of instant application (generic and genus) include the invention of USSN 09576,107 (species), issuance of a patent to the instant application would improperly extend the right to exclusivity. This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

It is noted that Applicants will respond by submission of an appropriate terminal disclaimer upon the event that conflicting claims issue from USSN 09/576,107 and the present application; the rejection is maintained.

9. The following new grounds of rejection are necessitated by the amendment filed 9/29/03.

10. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

11. Claim 35 is rejected under 35 U.S.C. 112, first paragraph, containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. **This is a new matter rejection**.

Claim 35 as written represents a departure from the specification and the claims as originally filed because the terms "spaced apart by an intervening sequence that does not include a methionine" and "minimal" have no support in the specification and the claims as originally filed.

12. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office Action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

13. Claim 35 is rejected under 35 U.S.C. 102(b) as being anticipated by Lawson et al (of record, J Virology 68(6): 3505-3511, June 1994, PTO 892).

Lawson *et al* teach recombinant vaccinia virus as an expression vector expressing the full-length polynucleotide of HA containing at least one CTL epitope (the full length inherently contains more than one CTL epitope) derived from a pathogen such as **influenza** virus and Adenovirus (leader sequence) (See page 3506, Materials and methods, in particular). The reference polynucleotide comprising the plurality of CTL epitopes is contiguous. The reference plurality of CTL epitopes are spaced apart by an intervening sequence that does not include a methionine and the reference polynucleotide inherently transcribed and then translated to the protein it encodes since said protein is effectively processed in vivo to induced H-2 K' restricted presentation and induction of NP-specific CTLs in BALB/c mice (See page 3508, Table 1, in particular). The term "substantially free of peptide sequence" as defined on page 2 at line 3-9 is to be taken as including such short lengths (e.g. 1-5 amino acids) of sequences naturally found to flank the cytotoxic T lymphocyte epitopes". The reference polynucleotide when delivered in vivo inherently transcribed, and translated into protein that it encodes and said protein inherently processed by antigen presenting cells in vivo to yield CTL epitope that permits effective HLA-restricted presentation and CTL induction because the inherent properties of the product cannot separate from the product. Thus, the reference teachings anticipate the claimed invention.

Applicants' arguments filed 9/29/03 have been fully considered but are not found persuasive.

Applicants' position is that claims 14 and 33 have been amended to recite each CTL epitopes is free of peptide sequences naturally found to flank that CTL epitopes". (2) The minimal CTL epitopes substantially free of flanking sequences in conjunction with the intervening sequence excludes a native protein as described by Lawson et al.

However, claim 35 still recites a polynucleotide comprising a nucleic acid sequence encoding a plurality of CTL epitope wherein each CTL epitope is "**substantially** free of peptide sequences naturally found to flank that CTL epitope". The specification defines on page 2 at line 3-9 that "substantially free of sequences naturally found to flank the cytotoxic T lymphocyte epitopes is to be taken as including such short lengths (e.g. 1-5 amino acids) of sequences naturally found to flank the cytotoxic T lymphocyte epitopes". Finally, the term "comprise" is open-ended. It expands the intervening sequence to include additional nucleotide at either or both ends of the intervening sequence. The term "comprising" is open-ended. It expands the CTL epitope to include additional amino acid residues, the corresponding nucleotide at either or both ends.

14. No claim is allowed.

15. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to "Neon" Phuong Huynh whose telephone number is (703) 308-4844 or (571) 272-0846 after January 20, 2004. The examiner can normally be reached Monday through Friday from 9:00 am to 6:00 p.m. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached at (703) 308-3973 or (571) 272-0841 after January 7, 2003. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

17. Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform to the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 872-9306.

Phuong N. Huynh, Ph.D.
Patent Examiner
Technology Center 1600
December 29, 2003

CHRISTINA CHAN
SUPERVISORY PATENT EXAMINER
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